IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant	: Constance A. Bell et al.	Art Unit	: 1637
Serial No.	: 10/068,238	Examiner	: Teresa E. Strzelecka
Filed	: February 5, 2002	Conf. No.	: 7696
Title	: DETECTION OF BACILLUS ANTHRACIS		

Mail Stop Appeal Brief - Patents
Commissioner for Patents
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REPLY BRIEF

Pursuant to 37 C.F.R. § 41.41, Applicants respond to the Examiner's Answer as indicated herein.

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Rejection Under 35 U.S.C. § 103(a)

Claims 57, 66, 67, 70, 79, 80, 83, 92, and 93 are not obvious.

As explained in detail in Applicant's Appeal Brief filed April 23, 2009, the combination of cited references fails to render claims 57, 66, 67, 70, 79, 80, 83, 92, and 93 obvious. The Examiner continues to assert that it would have been obvious to select a particular combination of nucleic acid sequences from published full-length *B. anthracis* genes and use them in real-time PCR to detect *B. anthracis*. The Examiner insists that Buck et al. demonstrates the "equivalence of primers" and "clearly shows that every primer would have a reasonable expectation of success" for any method of DNA amplification. (Examiner's Answer at page 6).

Applicants specifically selected the claimed pair of primers and pair of probes out of thousands of possibilities. The particular combination of primers and probes that Applicants' selected represents an important advancement over the state of the art, particularly in light of Applicants' comparative data demonstrating superior technical effect. The Federal Circuit has held that selection inventions, which claim a particular species from within a larger genus disclosed in the prior art, are not *prima facie* obvious where the claimed species was not specifically disclosed but rather part of a broad genus. See *In re Jones*, 958 F.2d 347 (Fed. Cir. 1992); *In re Baird*, 16 F.3d 380 (Fed. Cir. 1994). Accordingly, disclosure of the *capB*, *pagA* and *lef* sequences in the Makino et al., Price et al. and Bragg et al. references, respectively, does not render obvious the specifically-claimed primers and probes from each of those sequences.

Applicants further submit that the Examiner has misunderstood the nature of references submitted by Applicants. The references were not provided as "evidence that Applicants' primer selection was in any way unique" as the Examiner alleges. To the contrary, the references rebut the Examiner's assertion that Buck et al. is evidence that "EVERY SINGLE primer works." According to the Federal Circuit, Applicants may "attack the Examiner's *prima facie* determination as improperly made out." *In re Fritch*, 972 F.2d 1260, 1265 (Fed. Cir. 1992). As acknowledged in the Examiner's Answer (page 21), the Csordas et al. reference teaches poor performance of one set of primers and excellent performance of a second set. Significantly, the Csordas et al. reference discloses that "[p]rimers originally designed for end-point PCR did not have adequate specificity or sensitivity compared with those specifically designed for real-time

PCR." This reference as well as the other references provided by Applicants supports Applicants' assertion that all primers and probes are not equivalent, and that it is difficult to predict which primers are best suited for real-time PCR reactions. In sum, Applicants have provided evidence to rebut the Examiner's insistence based on Buck et al. that EVERY primer is guaranteed to work. To the contrary, primer and probe design for real-time PCR amplification is not always predictable, and a person of ordinary skill in the art would not have had a reasonable expectation of success in selecting a combination of a pair of primers and a pair of probes from the sequences disclosed in the cited references to use in real-time PCR to detect *B. anthracis*.

Applicants note that the Examiner cited *Ex parte Weisburg*, a BPAI decision, as Exhibit A in the Examiner's Answer, but did not provide any comments or reasons for citing this decision. Applicants respectfully submit that *Ex parte Weisburg* is not factually relevant to the present claims. The claims in *Ex parte Weisburg* are directed toward methods of detecting three different mycoplasma species using hybridization probes that are 10 to 250 nucleotides in length. Significantly, the claims in *Ex parte Weisburg* do not recite any specific sequences. Applicants further note that another recent Board decision (*Ex parte Kusama* (Appeal 2009-001929)) also is not factually relevant to the claims pending in the present application since the claims in *Kusama* do not recite both a pair of primers and a pair of probes. *Ex parte Kusama* only claims a pair of primers for use in conventional PCR and, as discussed above with respect to Csordas et al., a pair of primers for use in conventional PCR (or "end-point PCR" as used by Csordas et al.) is not predictive of success in a real-time PCR reaction.

Based on the arguments herein and the arguments already of record, Applicants respectfully request reversal of the Examiner's rejection of the pending claims under 35 U.S.C. §103.

Please apply any charges or credits to Deposit Account No. 06-1050.

Respectfully submitted,

/October 2, 2009/

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